UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/792,355	03/03/2004	Bruno Pfeiffer	SERVIER 396 PCT	5116

25666 7590 11/14/2006

THE FIRM OF HUESCHEN AND SAGE
SEVENTH FLOOR, KALAMAZOO BUILDING
107 WEST MICHIGAN AVENUE
KALAMAZOO, MI 49007

EXAMINER	
SHIAO, REI TSANG	
ART UNIT	**PAPER NUMBER**
1626	

DATE MAILED: 11/14/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/792,355	PFEIFFER ET AL.	
	Examiner	Art Unit	
	Robert Shiao	1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 August 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *14-26* is/are pending in the application.

4a) Of the above claim(s) *15-22 and 24* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *14,23,25 and 26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☒ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This Office action supersedes the previous Office action mailed on October 16, 2006.

1. This application claims benefit of the foreign application: FRANCE 00/08793 with a filing date 07/06/2000; and FRANCE 00/08973 with a filing date 07/06/2000. However, the foreign priority document FRANCE 00/08973 has not been filed to the Office. Applicants are requested to file the foreign priority document to the Office.

2. Applicant's arguments/remarks and a declaration under 37 CFR 1.132 filed on August 14, 2006, are acknowledged. Claims 14-26 are pending in the application.

Prior Art Rejections

3. In regards to the claimed compound, the prior art reference of Guez et al. WO 99/25374 or US 6,653,336 does not provide applicants' instant X-ray power diffraction data. However, Guez et al. do name the instant compound, which puts this product in the public domain, see Examples 1-2 on page 7 of Guez et al. '374 or see column 4 of Guez et al. '336. As these forms differ from the claims in that the reference are silent on the X-ray diffraction data, applicants must show that their crystalline form really is different from any crystalline forms prepared in the prior art. MPEP 2112 states: "Something which is old does not become patentable upon the discovery of a new property. The claiming of a new use, new function or unknown property which is inherently present in the prior art does not necessarily make the claim patentable, see *In*

re Best, 562 F.2d 1252, 1254, 195 USPQ 430, 433 (CCPA 1977). In this case, the "unknown property" is the particular crystalline form. This is unknown because the reference is silent on this property. MPEP 2112 goes on to state: "A rejection under 35 USC 102/103 can be made when the prior art product seems to be identical except that the prior art is silent as to an inherent characteristic. Where applicant claims a composition in terms of a function, property or characteristic and the compositions of the prior art is the same as that of the claim but the function is not explicitly disclosed by the reference, the examiner may make a rejection under both 35 USC 102 and 103, expressed as a 102/103 rejection." Here, the prior art is silent on is the X-ray diffraction pattern data. Nevertheless, this "characteristic" is inherent, therefore, explicit disclosure is not required.

Here the reference explicitly teaches the same compound. The only difference is a characteristic about which the reference happens to be silent, also see *Ex parte Anderson*, 21 USPQ 2nd 1241 and 1251. There, the decision states: "There is ample precedent for shifting the burden to an applicant to reproduce a prior art product whose final structure or properties are, at least, in part determined by the precise process used in its manufacture." (page 1253).

Responses to Arguments

4. Applicant's arguments regarding the rejection of claims 14, 23 and 25-26 over Vincent et al. '214 under 35 U.S.C. 102(b) or 103 (a) filed on August 14, 2006, have been fully considered and they are persuasive. Applicants argue that the instant α

crystalline compound of formula (I), i.e., perindopril of tert-butylamine salt, is distinct from Vincent et al., and distinctness between the instant α crystalline and prior art has been provided by Dr. Gerard Coquerel's declaration, and it is persuasive. The instant X-ray diffraction pattern data and stability data of α crystalline is distinct from Vincent et al. The rejection of claims 14, 23 and 25-26 over Vincent et al. '214 under 35 U.S.C. 102(b) or 103 (a) has been withdrawn herein. However, Guez et al. disclose the instant compound and its pharmaceutical compositions and are silent on the X-ray diffraction pattern data. Therefore, absent a showing of unobvious and superior properties in terms of mechanic benefits, the instant claimed compound/compositions of known compound/compositions would have been suggested to one skilled in the art. The rejection of claims of 25-26 over Guez et al. '336 under 35 U.S.C. 102(e), is maintained.

5. Applicant's arguments regarding the provisional rejection of claims 14, 23 and 25-26 under the obvious-type double patenting filed on August 14, 2006, have been fully considered and they are persuasive, in part. Since the instant X-ray diffraction pattern data of the α crystalline form is distinct form Pfeiffer et al. '489, the rejection of claim 14 under the obvious-type double patenting has been withdrawn herein. However, it is well recognized in the art that process of preparing pharmaceutical composition will produce the thermodynamically stable form of crystals, thus, Pfeiffer et al. β crystal form and the instant α crystalline form, after mixing, grinding, compressing would both be transformed into the same thermodynamically stable form(s) of the

instant form (i.e., α crystalline form), see Brittain's publication, pages 348-361. Therefore, the rejection of claims 23 and 25-26 under the obvious-type double patenting, is maintained. Applicants are requested to file a terminal disclaimer to overcome the rejection.

6. Applicant's arguments with respect to claims 14, 23, and 25-26 have been considered but are moot in view of the new ground(s) of rejection.

Claim Rejections - 35 USC § 112

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 23 and 25-26 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claims contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. It is well recognized in the art that process of preparing pharmaceutical composition will produce the thermodynamically stable form of crystals, thus, the instant α crystalline, after mixing, grinding, compressing would be transformed into a thermodynamically stable form(s), see Brittain's publication, pages 348-361.

In *In re Wands*, 8 USPQ2d 1400 (1988), factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first

paragraph, have been described. They are:

1. the nature of the invention,

2. the state of the prior art,

3. the predictability or lack thereof in the art,

4. the amount of direction or guidance present,

5. the presence or absence of working examples,

6. the breadth of the claims,

7. the quantity of experimentation needed, and

8. the level of the skill in the art.

In the instant case:

The nature of the invention

The nature of the invention is a pharmaceutical composition comprising a α crystalline form of perindopril, tert-butylamine salt, see claim 23.

The state of the prior art and the predictability or lack thereof in the art

The state of the prior art is that a similar pharmaceutical composition comprising the same compound perindopril, tert-butylamine salt. see Guez et al. WO 99/25374 or US 6,653,336.

The amount of direction or guidance present and the presence or absence of working examples

The only direction or guidance present in the instant specification is the general description of the instant pharmaceutical composition on page 4. There is no data present in the instant specification for the instant solid pharmaceutical composition, wherein the α crystalline form still exists after the process of preparation, i.e., mixing, grinding, and compressing.

The breadth of the claims

The instant breadth of the rejected claims lack enablement requirement, specifically, the instant solid pharmaceutical composition comprises the α crystalline form after processes of preparing pharmaceutical compositions.

The quantity or experimentation needed and the level of skill in the art

While the level of the skill in the chemical arts is high, it would require undue experimentation of one of ordinary skill in the art to resolve any solid pharmaceutical compositions, wherein the α crystalline form still exists after the processes of pharmaceutical preparation. There is no data present in the instant specification for the instant solid pharmaceutical compositions, wherein the α crystalline form still exists after the process of preparation, i.e., mixing, grinding, and compressing. Therefore, the claims lack enablement for the pharmaceutical composition comprising the α crystalline form. Dependent claims 25-26 are also rejected along with claim 23 under 35 U.S.C. 112, first paragraph.

Claim Rejections - 35 USC § 102

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 23 and 25-26 are rejected under 35 U.S.C. 102(b) as being anticipated by Guez et al. WO 99/25374.

Applicants claim a pharmaceutical composition comprising α crystalline form of perindopril, tert-butylamine salt, see claim 23. Dependent claims 25-26 further limit the instant pharmaceutical composition, i.e., it also comprises a diuretic.

Guez et al. disclose a pharmaceutical composition (i.e., injectable preparations, or aqueous solution) comprising the same compound perindopril, tert-butylamine salt, see lines 8-14 on page 5. It is noted that the injectable preparations can be water or aqueous solution and therefore the instant α crystalline forms of the instant compound dissolves in the composition (i.e., aqueous solution), and it will exist in free form and not as a crystal form. Therefore, the instant pharmaceutical composition is anticipated by Guez et al. Dependent claims 25-26 are also rejected along with claim 23 under 35 U.S.C. 102(b).

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in Graham v. John Deere Co., 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

10. Claims 14, 23 and 25-26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Guez et al. WO 99/25374.

Applicants claim a α crystalline form of perindopril, tert-butylamine salt

and its pharmaceutical compositions, see claims 14 and 23. Dependent claims 25-26 further limit the instant pharmaceutical composition, i.e., it also comprises a diuretic.

Determination of the scope and content of the prior art (MPEP §2141.01)

Guez et al. disclose the same instant compound of perindopril, tert-butylamine salt and its pharmaceutical composition, see pages 7-8, especially Examples 1-2 on page 8.

Determination of the difference between the prior art and the claims (MPEP §2141.02)

The difference between the instant claims and Guez et al. is that Guez et al. is silent on the X-ray diffraction data of the instant compound. It is noted that a crystalline form of a pure compound is an innate nature of a pure solid form.

Finding of prima facie obviousness-rational and motivation (MPEP §2142-2143)

One having ordinary skill in the art would find the instant claims 14, 23 and 25-26 prima facie obvious **because** one would be motivated to employ the compounds/ compositions of Guez et al. to obtain the instant compound and its pharmaceutical composition, wherein the instant compound is in a solid form (i.e., α crystalline form).

Further, changing the form, purity or other characteristic of an old product does not render the novel form patentable where the difference in form, purity or characteristic was inherent in or rendered obvious by the prior art, see *In re Cofer*, 148

U.S.P.Q. 268 (CCPA 1966). Therefore, absent a showing of unobvious and superior properties in terms of mechanic benefits, the instant claimed crystalline forms and its compositions of known compounds would have been suggested to one skilled in the art. Dependent claims 25-26 are also rejected along with claims 14 and 23 under 35 U.S.C. 103(a).

The motivation to obtain the claimed crystalline form of the compound perindopril, tert-butylamine salt or its pharmaceutical composition derives from known Guez et al. pharmaceutically useful compounds/compositions with the expectation of obtaining a pharmaceutically useful benefit, such as longer shelf life, stability, enhanced deliverability, etc., would possess similar activities (i.e., agents treating cardiovascular disease) to that which is claimed in the reference.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert Shiao whose telephone number is (571) 272-0707. The examiner can normally be reached on 8:30 AM - 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph K. McKane can be reached on (571) 272-0699. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information

for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Joseph K. McKane
Supervisory Patent Examiner
Art Unit 1626

R.S.

Robert Shiao, Ph.D.
Patent Examiner
Art Unit 1626

November 08, 2006